EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	19	"707848"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/11 17:42
L2	12	"613687"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/11 17:55
L3	1786	de haan	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	ADJ	OFF	2006/05/11 17:56
L4	49	l3 and akzo	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	ADJ	OFF	2006/05/11 18:07
L8	12	(("3340279") or ("4701450") or ("5037817") or ("4196188")).PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/05/11 18:16

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S168	0	insulin secretion and (appettite suppressant)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/08 15:07
S169	60	insulin secretion and (appetite suppressant)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/08 15:07
S171	37	de haan pieter	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 11:28
S172	9	S171 and tibolone	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 11:34
S173	21	pieter and tibolone	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 11:35
S175	2748	de haan	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:02
S176	0	"000513" and S175	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:02
S177	0	"0005513" and S175	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:02

EAST Search History

S178	12	S175 and tibolone	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:10
S179	499	S175 and "2001"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:11
S180	2748	S175 and ay="2001"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:11
S181	216	S175 and @ay="2001"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:12
S183	1	"de haan" and @ay="2001" and tibolone	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:12
S184	1	"6187339".PN.	USPAT; USOCR	NEAR	OFF	2006/05/09 16:14
S185	0	("6969708").URPN.	USPAT	NEAR	OFF	2006/05/09 16:16
S186	0	("2004/0229854").URPN.	USPAT	NEAR	OFF	2006/05/09 16:17
S187	0	("2004/0229854" | "2006/0051420" | "6399594" | "6514958" | "6969708").URPN.	USPAT	NEAR	OFF	2006/05/09 16:17
S190	1	"de haan" and @ay="2001" and menopau$	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/09 16:19

EAST Search History

S192	43	haan pieter	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	NEAR	OFF	2006/05/10 17:07

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Dialog level 05.11.05D

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Logon file001 10may06 06:34:23
           *** ANNOUNCEMENTS ***
                    ***
NEW FILES RELEASED
***Regulatory Affairs Journals (File 183)
***Index Chemicus (File 302)
***Inspec (File 202)

RESUMED UPDATING
***File 141, Reader's Guide Abstracts
                    ***
RELOADS COMPLETED
***File 516, D&B--Dun's Market Identifiers
***File 523, D&B European Dun's Market Identifiers
***File 531, American Business Directory
*** MEDLINE has been reloaded with the 2006 MeSH (Files 154 & 155)
*** The 2005 reload of the CLAIMS files (Files 340, 341, 942)
is now available online.
                                    ***
DATABASES REMOVED
***File 196, FINDEX
***File 468, Public Opinion Online (POLL)

Chemical Structure Searching now available in Prous Science Drug
Data Report (F452), Prous Science Drugs of the Future (F453),
IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein
Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus
(File 302).
                    ***
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 >>>a specific database by entering HELP NEWS <file number>.<<<
* * *

File   1:ERIC 1966-2006/Mar (c) format only 2006 Dialog

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     $0.40  Estimated cost File1
     $1.06  TELNET
     $1.46  Estimated cost this search
     $1.46  Estimated total session cost   0.114 DialUnits


SYSTEM:OS  - DIALOG OneSearch
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         (c) 2006 BIOSIS
  File  34:SciSearch(R) Cited Ref Sci 1990-2006/Apr W5
         (c) 2006 Inst for Sci Info
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File 155:MEDLINE(R) 1951-2006/May 12
(c) format only 2006 Dialog
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
(c) 1998 Inst for Sci Info

Set	Items	Description

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          1038054  RELEASE
      S3       20  S2 AND RELEASE
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Processing
             9  S4
      44715778  PY<=2000
      S5        3  S4 AND PY<=2000
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5/9/1 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

0012765852 BIOSIS NO.: 200000484165

Gender differences and the effects of synthetic exogenous and non-synthetic estrogens in focal cerebral ischemia

AUTHOR: Vergouwen Mervyn D I; Anderson Robert E (Reprint); Meyer Fredric B
AUTHOR ADDRESS: Department of Neurosurgery, Mayo Clinic, 200 First Street SW, Rochester, MN, 55905, USA**USA

JOURNAL: Brain Research 878 (1-2): p88-97 29 SEPTEMBER, 2000 **2000**
MEDIUM: print
ISSN: 0006-8993
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The role of gender difference and estrogen in ischemic cerebrovascular events is controversial. Evidence is lacking as to whether or not there are significant gender differences in the incidence and outcome of stroke in the clinical setting. Recent clinical epidemiological studies have demonstrated that there is no significant association between the use of hormonal replacement therapy and the risk of stroke. However, several animal studies have shown that there are gender differences in stroke outcome and that exogenous administered estrogens are neuroprotective. In this study, the influence of gender differences and the effects of synthetic and non-synthetic estrogens were examined in a model of focal cerebral ischemia using 210 male, intact female, and ovariectomized female rats. All animals underwent 3 h of middle cerebral artery and bilateral common carotid artery occlusion. After 72 h, the rats were sacrificed and stained for histological assessment of infarction. There were no gender differences in infarction volume. Intravenous administration of either low or high dose 17beta-estradiol or **tibolone** did not alter infarct volume. Subcutaneous administration of low and high dose 17beta-estradiol using 7-day **release** pellets did not alter infarct volume. Low dose **tibolone** using implanted 7-day **release** pellets did not alter infarct volume. However,

high dose **tibolone** using implanted 7-day **release** pellets significantly (P<0.05) reduced infarct volume only in ovariectomized female rats. These results demonstrate that estrogen therapy has no effect on infarction volume following severe focal cerebral ischemia.

REGISTRY NUMBERS: 50-28-2: 17-beta-estradiol; 5630-53-5: **tibolone**
DESCRIPTORS:
MAJOR CONCEPTS: Nervous System--Neural Coordination; Pharmacology; Cardiovascular System--Transport and Circulation
BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: rat (Muridae)--animal model, female, male
COMMON TAXONOMIC TERMS: Animals; Chordates; Mammals; Nonhuman Vertebrates ; Nonhuman Mammals; Rodents; Vertebrates
DISEASES: focal cerebral ischemia--nervous system disease, vascular disease; stroke--nervous system disease, vascular disease, incidence, outcome
MESH TERMS: Brain Ischemia (MeSH); Cerebrovascular Disorders (MeSH)
CHEMICALS & BIOCHEMICALS: 17-beta-estradiol; synthetic exogenous estrogen; **tibolone**
METHODS & EQUIPMENT: hormone replacement therapy--therapeutic method
MISCELLANEOUS TERMS: sex difference
CONCEPT CODES:
20506 Nervous system - Pathology
10067 Biochemistry studies - Sterols and steroids
12512 Pathology - Therapy
14504 Cardiovascular system - Physiology and biochemistry
14508 Cardiovascular system - Blood vessel pathology
20504 Nervous system - Physiology and biochemistry
22002 Pharmacology - General
BIOSYSTEMATIC CODES:
86375 Muridae

5/9/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011215837 BIOSIS NO.: 199800010084
Modulatory effects of a synthetic steroid (tibolone) and estradiol on spontaneous and GH-RH-induced GH secretion in postmenopausal women
AUTHOR: Genazzani Alessandro D (Reprint); Gamba Ombretta; Nappi Luigi; Volpe Annibale; Petraglia Felice
AUTHOR ADDRESS: Physiopathol. Human Reproduct., Univ. Modena, Via del Pozzo 71, 41 100 Modena, Italy**Italy
JOURNAL: Maturitas 28 (1): p27-33 Sept., 1997 **1997**
MEDIUM: print
ISSN: 0378-5122
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Objective: Since hormonal replacement therapy (HRT) affects plasma GH levels, the present study aimed to verify the effect of **tibolone** , a synthetic steroid, on modulating spontaneous and growth hormone releasing hormone (GH-RH) induced GH secretion. Methods: Postmenopausal women (n=30) were enrolled and randomly subdivided in three groups (n=10 each group): (1) treated with transdermal estradiol (50 mug) (Dermestrill, Rottapharm, Monza, Italy) biweekly; (2) treated with transdermal estradiol (100 mug) (Dermestrill. Rottapharm, Monza,

Italy) biweekly; (3) treated with **tibolone** 2.5 mg/day (Livial, Organon Italia, Rome, Italy). Patients underwent a GH-RH test (1 mug/kg) and 15 of them underwent to a pulsatility study before and 5 weeks after treatment. Results: Mean(+S.E.M.) GH plasma levels increased in all patients after any type of HRT. GH response to GH-RH stimulation (expressed as maximal response to GH-RH or as delta value) was similar in the three groups while significant changes occurred in spontaneous pulsatile GH **release** . **Tibolone** and both dosages of transdermal estradiol significantly reduced GH pulse frequency and increased pulse amplitude. Conclusions: The reduced plasma GH levels observed during postmenopause are probably related to a reduced endogenous GH-RH and not to a reduced pituitary ability to respond to GH-RH. In addition **tibolone** , as well as transdermal estradiol, are effective in restoring the spontaneous GH episodic **release.**

REGISTRY NUMBERS: 50-28-2: estradiol; 5630-53-5: **tibolone**
DESCRIPTORS:
MAJOR CONCEPTS: Clinical Endocrinology--Human Medicine, Medical Sciences; Pharmacology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)--female, patient, postmenopausal
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates
CHEMICALS & BIOCHEMICALS: estradiol--estrogen-drug, hormone-drug, modulatory effects; **tibolone** --estrogen-drug, modulatory effects, synthetic steroid
METHODS & EQUIPMENT: hormonal replacement therapy--therapeutic method
MISCELLANEOUS TERMS: growth hormone-releasing hormone-induced growth hormone secretion; pulsatile growth hormone **release**
CONCEPT CODES:
22002 Pharmacology - General
10060 Biochemistry studies - General
16501 Reproductive system - General and methods
17002 Endocrine - General
BIOSYSTEMATIC CODES:
86215 Hominidae

5/9/3 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03947633 Genuine Article#: QU412 Number of References: 67
Title: A COMPARATIVE-STUDY OF 2 HORMONE REPLACEMENT THERAPY REGIMENS ON SAFETY AND EFFICACY VARIABLES
Author(s): SISELES NO; HALPERIN H; BENENCIA HJ; BERG G; PILNIK S; MESCH V; ARRIGHI B; WIKINSKI RWW
Corporate Source: HOSP ITALIANO BUENOS AIRES,DIV GYNECOL,CLIMACTER SECT,ARAOZ 2241 PISO 3 C/BUENOS AIRES/DF/ARGENTINA/; HOSP FRANCES RIOSA/BUENOS AIRES/DF/ARGENTINA/; UNIV BUENOS AIRES,DEPT CLIN BIOCHEM/BUENOS AIRES/DF/ARGENTINA/
Journal: MATURITAS, **1995** , V21, N3 (APR), P201-210
ISSN: 0378-5122
Language: ENGLISH Document Type: ARTICLE
Geographic Location: ARGENTINA
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences; CC CLIN--Current Contents, Clinical Medicine
Journal Subject Category: GERIATRICS & GERONTOLOGY; OBSTETRICS & GYNECOLOGY ; MEDICINE, GENERAL & INTERNAL

Abstract: Objective: To assess the effect of **tibolone** on endometrial safety, plasma estradiol concentrations, lipid metabolism and climacteric symptoms in comparison to sequential conjugated equine estrogens and medroxyprogesterone acetate in postmenopausal women. Methods: In a randomised, open-label, 6-cycle, group-comparative study, the effects on the aforementioned parameters were studied with **tibolone** 2.5 mg/day (N= 13) continuously, and with conjugated equine estrogens 0.625 mg/day continuously, combined with medroxyprogesterone acetate 5 mg/day (N=11) (CEE/MPA) sequentially, during 12 days of each 28-day cycle. Within-group statistical analysis was performed with Student's t-test for paired samples, whereas between-group statistics were performed using the Student's t-test for independent groups. Results: Cytological evaluation revealed no endometrial stimulation in either group. In the **tibolone** group, there were no effects on estradiol levels, whereas in the CEE/MPA group, an increase in total and non-SHBG-bound estradiol plasma levels was reported. In the **tibolone** group, there were significant decreases in plasma total cholesterol, triglycerides, HDL-cholesterol and VLDL-cholesterol, whereas no significant changes in LDL-cholesterol and IDL-cholesterol were reported. In the CEE/MPA group there were significant decreases in plasma total cholesterol, HDL-cholesterol and LDL-cholesterol, whereas there were no significant changes in triglycerides,IDL-cholesterol and VLDL-cholesterol. Climacteric symptoms, particularly vasomotor episodes, decreased similarly in both groups. Conclusions: Both **tibolone** and CEE/MPA were safe with respect to effects on the endometrium and both treatments induced changes in the plasma profiles of certain lipid and lipoprotein parameters. However, the overall clinical implications of these changes are unknown. Finally, both regimens were equally effective in the treatment of climacteric symptoms.
Descriptors--Author Keywords: **TIBOLONE** ; CONJUGATED EQUINE ESTROGENS ; MEDROXYPROGESTERONE ACETATE ; ESTROGEN ; LIPIDS ; CLIMACTERIC SYMPTOMS
Identifiers--KeyWords Plus: INTERMEDIATE-DENSITY LIPOPROTEINS; CHOLESTEROL-FED RABBITS; POSTMENOPAUSAL WOMEN; ENDOMETRIAL CANCER; POST-MENOPAUSAL; AORTIC ACCUMULATION; ESTROGEN THERAPY; INCREASED RISK; DOUBLE-BLIND; ORG OD-14
Research Fronts: 93-1862 001 (HORMONE REPLACEMENT THERAPY; POSTMENOPAUSAL WOMEN; PERORAL ESTROGEN SUBSTITUTION)
93-4872 001 (TRANSDERMAL ESTROGEN REPLACEMENT THERAPY; POSTMENOPAUSAL WOMEN; SUSTAINED- **RELEASE** SUBDERMAL ESTRADIOL IMPLANTS)
93-5772 001 (ENDOMETRIAL CANCER IN POSTMENOPAUSAL WOMEN; BODY-MASS INDEX; PREVALENCE OF OBESITY; RISK FOR CARDIOVASCULAR-DISEASE; PROGNOSTIC FACTORS; BRITISH ELDERLY)
Cited References:
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BARBO DM, 1987, V71, P11, MED CLIN N AM
BARENTSEN R, 1993, V51, P203, EUR J OBSTET GYN R B
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CUMMING DC, 1985, V61, P873, J CLIN ENDOCR METAB
CUST MP, 1990, V5, P345, DRUG SAFETY
DAWOOD MY, 1986, V155, P1246, AM J OBSTET GYNECOL
DEVISSER J, 1984, V34, P1010, ARZNEIMITTEL-FORSCH
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GENAZZANI AR, 1991, V13, P243, MATURITAS
GENAZZANI AR, 1987, V1, P35, MATURITAS S1
HAARBO J, 1992, V70, P1198, CIRC RES
HAARBO J, 1991, V87, P1274, J CLIN INVEST
HAENGGI W, 1993, V31, P645, EUR J CLIN CHEM CLIN
HAHN RG, 1989, V161, P1854, AM J OBSTET GYNECOL
HARDIMAN P, 1991, V13, P235, MATURITAS
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HUNT K, 1990, V97, P1080, BRIT J OBSTET GYNAEC
KABLE WT, 1990, V35, P512, J REPROD MED
KICOVIC PM, 1982, V6, P81, REPRODUCCION
KLOOSTERBOER HJ, 1990, V12, P37, MATURITAS
KUPPERMAN HS, 1953, V6, P688, J CLIN ENDOCRINOL
LAPOLLA JP, 1990, V163, P1055, AM J OBSTET GYNECOL
LEFFLER H, 1963, V39, P313, AM J CLIN PATHOL
LEHMANN ED, 1994, V67, P701, BRIT J RADIOL
LINDSAY R, 1980, V280, P1207, BRIT MED J
LUCIANO AA, 1993, V38, P207, J REPROD MED
MACK TM, 1976, V294, P1262, NEW ENGL J MED
MCBRIDE JM, 1954, V61, P691, J OBSTET GYN BR COMM
OMODEI U, 1990, 46TH ANN M AM FERT S
PALERMO VG, 1985, V65, P271, OBSTET GYNECOL
PARDRIDGE WM, 1986, V15, P259, CLIN ENDOCRINOL META
PERSSON I, 1989, V298, P147, BRIT MED J
POWERS MS, 1985, V152, P1099, AM J OBSTET GYNECOL
PUNNONEN R, 1984, V5, P281, MATURITAS
RIJPKEMA AHM, 1990, V12, P259, MATURITAS
RYMER J, 1993, V128, P259, ACTA ENDOCRINOL-COP
SENTI M, 1992, V85, P30, CIRCULATION
SHERWIN BB, 1989, V73, P759, OBSTET GYNECOL
SISELES NO, 1990, 6TH INT C MEN BANGK
SITRUKWARE R, 1990, V39, P203, DRUGS
SMITH DC, 1975, V293, P1164, NEW ENGL J MED
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STUMPF PG, 1981, V52, P138, J CLIN ENDOCR METAB
TAX L, 1987, V1, P3, MATURITAS S
UTIAN WH, 1989, V161, P1828, AM J OBSTET GYNECOL
VOLPE A, 1986, V8, P327, MATURITAS
WEINSTEIN L, 1987, V69, P929, OBSTET GYNECOL
WHITEHEAD M, 1988, V2, P1243, LANCET
WHITEHEAD MI, 1979, V72, P322, J ROY SOC MED
WIELAND H, 1973, V19, P1139, CLIN CHEM
WIELAND H, 1983, V24, P904, J LIPID RES
WIKINSKI RLW, 1991, V37, P1913, CLIN CHEM
WITTEMAN JCM, 1989, V298, P642, BRIT MED J
ZIEL HK, 1975, V293, P1167, NEW ENGL J MED

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S4           9   RD  (unique items)
S5           3   S4 AND PY<=2000
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Welcome to DIALOG

Dialog level 05.11.05D

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Logon file001 10may06 06:34:23
           *** ANNOUNCEMENTS ***
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***Index Chemicus (File 302)
***Inspec (File 202)

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***File 523, D&B European Dun's Market Identifiers
***File 531, American Business Directory
*** MEDLINE has been reloaded with the 2006 MeSH (Files 154 & 155)
*** The 2005 reload of the CLAIMS files (Files 340, 341, 942)
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***File 196, FINDEX
***File 468, Public Opinion Online (POLL)

Chemical Structure Searching now available in Prous Science Drug
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IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein
Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus
(File 302).
                    ***
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* * *

File   1:ERIC 1966-2006/Mar (c) format only 2006 Dialog

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Terminal set to DLINK
? b 5,34, 155, 434
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            $0.40    0.114 DialUnits File1
     $0.40  Estimated cost File1
     $1.06  TELNET
     $1.46  Estimated cost this search
     $1.46  Estimated total session cost   0.114 DialUnits


SYSTEM:OS  - DIALOG OneSearch
  File   5:Biosis Previews(R) 1969-2006/May W1
         (c) 2006 BIOSIS
  File  34:SciSearch(R) Cited Ref Sci 1990-2006/Apr W5
         (c) 2006 Inst for Sci Info
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  File 155:MEDLINE(R) 1951-2006/May 12
         (c) format only 2006 Dialog
  File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info

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? s tibolone
      S2    1659  TIBOLONE
? s s2 and release
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         1038054  RELEASE
      S3      20  S2 AND RELEASE
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? s s4 and py<=2000
Processing
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? t s5/full/all

 5/9/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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0012765852   BIOSIS NO.: 200000484165
Gender differences and the effects of synthetic exogenous and non-synthetic
  estrogens in focal cerebral ischemia
AUTHOR: Vergouwen Mervyn D I; Anderson Robert E (Reprint); Meyer Fredric B
AUTHOR ADDRESS: Department of Neurosurgery, Mayo Clinic, 200 First Street
  SW, Rochester, MN, 55905, USA**USA
JOURNAL: Brain Research  878 (1-2): p88-97 29 SEPTEMBER, 2000  2000
MEDIUM: print
ISSN: 0006-8993
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The role of gender difference and estrogen in ischemic
  cerebrovascular events is controversial. Evidence is lacking as to
  whether or not there are significant gender differences in the incidence
  and outcome of stroke in the clinical setting. Recent clinical
  epidemiological studies have demonstrated that there is no significant
  association between the use of hormonal replacement therapy and the risk
  of stroke. However, several animal studies have shown that there are
  gender differences in stroke outcome and that exogenous administered
  estrogens are neuroprotective. In this study, the influence of gender
  differences and the effects of synthetic and non-synthetic estrogens were
  examined in a model of focal cerebral ischemia using 210 male, intact
  female, and ovariectomized female rats. All animals underwent 3 h of
  middle cerebral artery and bilateral common carotid artery occlusion.
  After 72 h, the rats were sacrificed and stained for histological
  assessment of infarction. There were no gender differences in infarction
  volume. Intravenous administration of either low or high dose
  17beta-estradiol or  tibolone  did not alter infarct volume. Subcutaneous
  administration of low and high dose 17beta-estradiol using 7-day  release
   pellets did not alter infarct volume. Low dose  tibolone  using
  implanted 7-day  release  pellets did not alter infarct volume. However,
```

high dose **tibolone** using implanted 7-day **release** pellets significantly (P<0.05) reduced infarct volume only in ovariectomized female rats. These results demonstrate that estrogen therapy has no effect on infarction volume following severe focal cerebral ischemia.

REGISTRY NUMBERS: 50-28-2: 17-beta-estradiol; 5630-53-5: **tibolone**
DESCRIPTORS:
MAJOR CONCEPTS: Nervous System--Neural Coordination; Pharmacology; Cardiovascular System--Transport and Circulation
BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: rat (Muridae)--animal model, female, male
COMMON TAXONOMIC TERMS: Animals; Chordates; Mammals; Nonhuman Vertebrates ; Nonhuman Mammals; Rodents; Vertebrates
DISEASES: focal cerebral ischemia--nervous system disease, vascular disease; stroke--nervous system disease, vascular disease, incidence, outcome
MESH TERMS: Brain Ischemia (MeSH); Cerebrovascular Disorders (MeSH)
CHEMICALS & BIOCHEMICALS: 17-beta-estradiol; synthetic exogenous estrogen; **tibolone**
METHODS & EQUIPMENT: hormone replacement therapy--therapeutic method
MISCELLANEOUS TERMS: sex difference
CONCEPT CODES:
20506 Nervous system - Pathology
10067 Biochemistry studies - Sterols and steroids
12512 Pathology - Therapy
14504 Cardiovascular system - Physiology and biochemistry
14508 Cardiovascular system - Blood vessel pathology
20504 Nervous system - Physiology and biochemistry
22002 Pharmacology - General
BIOSYSTEMATIC CODES:
86375 Muridae

5/9/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011215837 BIOSIS NO.: 199800010084
Modulatory effects of a synthetic steroid (tibolone) and estradiol on spontaneous and GH-RH-induced GH secretion in postmenopausal women
AUTHOR: Genazzani Alessandro D (Reprint); Gamba Ombretta; Nappi Luigi; Volpe Annibale; Petraglia Felice
AUTHOR ADDRESS: Physiopathol. Human Reproduct., Univ. Modena, Via del Pozzo 71, 41 100 Modena, Italy**Italy
JOURNAL: Maturitas 28 (1): p27-33 Sept., 1997 **1997**
MEDIUM: print
ISSN: 0378-5122
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Objective: Since hormonal replacement therapy (HRT) affects plasma GH levels, the present study aimed to verify the effect of **tibolone** , a synthetic steroid, on modulating spontaneous and growth hormone releasing hormone (GH-RH) induced GH secretion. Methods: Postmenopausal women (n=30) were enrolled and randomly subdivided in three groups (n=10 each group): (1) treated with transdermal estradiol (50 mug) (Dermestrill, Rottapharm, Monza, Italy) biweekly; (2) treated with transdermal estradiol (100 mug) (Dermestrill. Rottapharm, Monza,

Italy) biweekly; (3) treated with **tibolone** 2.5 mg/day (Livial, Organon Italia, Rome, Italy). Patients underwent a GH-RH test (1 mug/kg) and 15 of them underwent to a pulsatility study before and 5 weeks after treatment. Results: Mean(+S.E.M.) GH plasma levels increased in all patients after any type of HRT. GH response to GH-RH stimulation (expressed as maximal response to GH-RH or as delta value) was similar in the three groups while significant changes occurred in spontaneous pulsatile GH **release** . **Tibolone** and both dosages of transdermal estradiol significantly reduced GH pulse frequency and increased pulse amplitude. Conclusions: The reduced plasma GH levels observed during postmenopause are probably related to a reduced endogenous GH-RH and not to a reduced pituitary ability to respond to GH-RH. In addition **tibolone** , as well as transdermal estradiol, are effective in restoring the spontaneous GH episodic **release.**

REGISTRY NUMBERS: 50-28-2: estradiol; 5630-53-5: **tibolone**
DESCRIPTORS:
MAJOR CONCEPTS: Clinical Endocrinology--Human Medicine, Medical Sciences; Pharmacology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)--female, patient, postmenopausal
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates
CHEMICALS & BIOCHEMICALS: estradiol--estrogen-drug, hormone-drug, modulatory effects; **tibolone** --estrogen-drug, modulatory effects, synthetic steroid
METHODS & EQUIPMENT: hormonal replacement therapy--therapeutic method
MISCELLANEOUS TERMS: growth hormone-releasing hormone-induced growth hormone secretion; pulsatile growth hormone **release**
CONCEPT CODES:
22002 Pharmacology - General
10060 Biochemistry studies - General
16501 Reproductive system - General and methods
17002 Endocrine - General
BIOSYSTEMATIC CODES:
86215 Hominidae

5/9/3 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03947633 Genuine Article#: QU412 Number of References: 67
Title: A COMPARATIVE-STUDY OF 2 HORMONE REPLACEMENT THERAPY REGIMENS ON SAFETY AND EFFICACY VARIABLES
Author(s): SISELES NO; HALPERIN H; BENENCIA HJ; BERG G; PILNIK S; MESCH V; ARRIGHI B; WIKINSKI RWW
Corporate Source: HOSP ITALIANO BUENOS AIRES,DIV GYNECOL,CLIMACTER SECT,ARAOZ 2241 PISO 3 C/BUENOS AIRES/DF/ARGENTINA/; HOSP FRANCES RIOSA/BUENOS AIRES/DF/ARGENTINA/; UNIV BUENOS AIRES,DEPT CLIN BIOCHEM/BUENOS AIRES/DF/ARGENTINA/
Journal: MATURITAS, **1995** , V21, N3 (APR), P201-210
ISSN: 0378-5122
Language: ENGLISH Document Type: ARTICLE
Geographic Location: ARGENTINA
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences; CC CLIN--Current Contents, Clinical Medicine
Journal Subject Category: GERIATRICS & GERONTOLOGY; OBSTETRICS & GYNECOLOGY ; MEDICINE, GENERAL & INTERNAL

Abstract: Objective: To assess the effect of **tibolone** on endometrial safety, plasma estradiol concentrations, lipid metabolism and climacteric symptoms in comparison to sequential conjugated equine estrogens and medroxyprogesterone acetate in postmenopausal women. Methods: In a randomised, open-label, 6-cycle, group-comparative study, the effects on the aforementioned parameters were studied with **tibolone** 2.5 mg/day (N= 13) continuously, and with conjugated equine estrogens 0.625 mg/day continuously, combined with medroxyprogesterone acetate 5 mg/day (N=11) (CEE/MPA) sequentially, during 12 days of each 28-day cycle. Within-group statistical analysis was performed with Student's t-test for paired samples, whereas between-group statistics were performed using the Student's t-test for independent groups. Results: Cytological evaluation revealed no endometrial stimulation in either group. In the **tibolone** group, there were no effects on estradiol levels, whereas in the CEE/MPA group, an increase in total and non-SHBG-bound estradiol plasma levels was reported. In the **tibolone** group, there were significant decreases in plasma total cholesterol, triglycerides, HDL-cholesterol and VLDL-cholesterol, whereas no significant changes in LDL-cholesterol and IDL-cholesterol were reported. In the CEE/MPA group there were significant decreases in plasma total cholesterol, HDL-cholesterol and LDL-cholesterol, whereas there were no significant changes in triglycerides,IDL-cholesterol and VLDL-cholesterol. Climacteric symptoms, particularly vasomotor episodes, decreased similarly in both groups. Conclusions: Both **tibolone** and CEE/MPA were safe with respect to effects on the endometrium and both treatments induced changes in the plasma profiles of certain lipid and lipoprotein parameters. However, the overall clinical implications of these changes are unknown. Finally, both regimens were equally effective in the treatment of climacteric symptoms.
Descriptors--Author Keywords: **TIBOLONE** ; CONJUGATED EQUINE ESTROGENS ; MEDROXYPROGESTERONE ACETATE ; ESTROGEN ; LIPIDS ; CLIMACTERIC SYMPTOMS
Identifiers--KeyWords Plus: INTERMEDIATE-DENSITY LIPOPROTEINS; CHOLESTEROL-FED RABBITS; POSTMENOPAUSAL WOMEN; ENDOMETRIAL CANCER; POST-MENOPAUSAL; AORTIC ACCUMULATION; ESTROGEN THERAPY; INCREASED RISK; DOUBLE-BLIND; ORG OD-14
Research Fronts: 93-1862 001 (HORMONE REPLACEMENT THERAPY; POSTMENOPAUSAL WOMEN; PERORAL ESTROGEN SUBSTITUTION)
93-4872 001 (TRANSDERMAL ESTROGEN REPLACEMENT THERAPY; POSTMENOPAUSAL WOMEN; SUSTAINED- **RELEASE** SUBDERMAL ESTRADIOL IMPLANTS)
93-5772 001 (ENDOMETRIAL CANCER IN POSTMENOPAUSAL WOMEN; BODY-MASS INDEX; PREVALENCE OF OBESITY; RISK FOR CARDIOVASCULAR-DISEASE; PROGNOSTIC FACTORS; BRITISH ELDERLY)
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BARENTSEN R, 1993, V51, P203, EUR J OBSTET GYN R B
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HAENGGI W, 1993, V31, P645, EUR J CLIN CHEM CLIN
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KABLE WT, 1990, V35, P512, J REPROD MED
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PARDRIDGE WM, 1986, V15, P259, CLIN ENDOCRINOL META
PERSSON I, 1989, V298, P147, BRIT MED J
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PUNNONEN R, 1984, V5, P281, MATURITAS
RIJPKEMA AHM, 1990, V12, P259, MATURITAS
RYMER J, 1993, V128, P259, ACTA ENDOCRINOL-COP
SENTI M, 1992, V85, P30, CIRCULATION
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STUMPF PG, 1981, V52, P138, J CLIN ENDOCR METAB
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WITTEMAN JCM, 1989, V298, P642, BRIT MED J
ZIEL HK, 1975, V293, P1167, NEW ENGL J MED

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Set	Items	Description
S1	0	TIOBOLONE
S2	1659	TIBOLONE
S3	20	S2 AND RELEASE
S4	9	RD (unique items)
S5	3	S4 AND PY<=2000

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File   1:ERIC 1966-2006/Mar (c) format only 2006 Dialog

      Set  Items  Description
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Cost is in DialUnits
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Terminal set to DLINK
? b 5, 155
       10may06 06:42:24 User291213 Session D13.1
            $0.37    0.105 DialUnits File1
     $0.37  Estimated cost File1
     $0.11  TELNET
     $0.48  Estimated cost this search
     $0.48  Estimated total session cost   0.105 DialUnits


SYSTEM:OS  - DIALOG OneSearch
  File   5:Biosis Previews(R) 1969-2006/May W1
         (c) 2006 BIOSIS
  File 155:MEDLINE(R) 1951-2006/May 12
         (c) format only 2006 Dialog

      Set  Items  Description
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? s particle()size
          115385  PARTICLE
          843597  SIZE
      S1   39949  PARTICLE()SIZE
? s drug()release
         5058211  DRUG
          634193  RELEASE
      S2    9496  DRUG()RELEASE
? s s1 and s2
           39949  S1
            9496  S2
      S3    1119  S1 AND S2
? s immediate()release or fast()release
          168847  IMMEDIATE
          634193  RELEASE
            2163  IMMEDIATE(W)RELEASE
          198598  FAST
          634193  RELEASE
             552  FAST(W)RELEASE
      S4    2714  IMMEDIATE()RELEASE OR FAST()RELEASE
? s s1 and s2 and s3
           39949  S1
            9496  S2
            1119  S3
      S5    1119  S1 AND S2 AND S3
? s oral or peroral
          737586  ORAL
            5841  PERORAL
      S6  741667  ORAL OR PERORAL
? s oral or peroral or tablet?
          737586  ORAL
            5841  PERORAL
           49590  TABLET?
      S7  779168  ORAL OR PERORAL OR TABLET?
? s s1 and s2 and s4 and s7
           39949  S1
            9496  S2
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           2714  S4
         779168  S7
      S8       8  S1 AND S2 AND S4 AND S7
? rd
      S9       6  RD  (unique items)
? s s9 and py<=2001
              6  S9
       26962318  PY<=2001
     S10       3  S9 AND PY<=2001
? t s10/full/all

 10/9/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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0012115461   BIOSIS NO.: 199900375121
Design and characterization of a surfactant-enriched tablet formulation
  for oral delivery of a poorly water-soluble immunosuppressive agent
AUTHOR: Ruddy Stephen B (Reprint); Matuszewska Bozena K; Grim Yvetta A;
  Ostovic Drazen; Storey David E
AUTHOR ADDRESS: Department of Pharmaceutical Research, Merck Research
  Laboratories, Merck and Co. Inc., WP78A-31, West Point, PA, 19486, USA**
  USA
JOURNAL: International Journal of Pharmaceutics (Amsterdam)  182 (2): p
173-186 May 25, 1999  1999
MEDIUM: print
ISSN: 0378-5173
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The feasibility of incorporating significant quantities of the
  anionic surfactant, sodium lauryl sulfate (SDS), into an immediate
  release tablet formulation of a poorly water-soluble immunosuppressive
  agent was investigated. Despite the extremely poor compressibility of SDS
  and poor chemical stability of the drug, a commercializable,
  direct-compression tablet formulation with satisfactory mechanical
  properties and acceptable chemical stability was achieved. Optimal in
  vitro release of the drug from the tablet formulation was achieved by
  establishing the minimum molar uptake ratio necessary to achieve complete
  micellar solubilization of the drug, after which formulation studies were
  conducted to determine the influence of formulation and process variables
  on the rate and extent of drug release . A model-independent analysis
  of dissolution results in a reduced volume (250 ml) of modified simulated
  gastric fluid demonstrated that the rate and extent of drug release
  was highly dependent onthe mean particle size of the bulk drug, but
  independent of compression force above that required to achieve a compact
  of acceptable mechanical strength. Employing the Korsmeyer-Peppas model
  of Fickian and non-Fickian drug release , it was further shown that
  release of the drug from the dosage form was governed largely by surface
  erosion of the surfactant-enriched tablet matrix.

REGISTRY NUMBERS: 151-21-3: sodium lauryl sulfate
DESCRIPTORS:
  MAJOR CONCEPTS: Chemistry; Pharmaceuticals--Pharmacology
  CHEMICALS & BIOCHEMICALS:  sodium lauryl sulfate--surfactant; L-733,725
    --immunosuppressant-drug, in-vitro release,  micellar solubilization,
    surfactant-enriched tablet formulation,  oral delivery,  poorly
    water-soluble
CONCEPT CODES:
```

22002 Pharmacology - General
10060 Biochemistry studies - General

10/9/2 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12702315 PMID: 10794929
Application of Carbopol to controlled release preparations I. Carbopol as a novel coating material.
Muramatsu M; Kanada K; Nishida A; Ouchi K; Saito N; Yoshida M; Shimoaka A ; Ozeki T; Yuasa H; Kanaya Y
Pharmaceutical Laboratories, Kissei Pharmaceutical Company, Limited, 4365-1 Kashiwabara, Hotaka, Minamiazumi, Nagano, Japan.
International journal of pharmaceutics (NETHERLANDS) Apr 10 **2000** , 199 (1) p77-83, ISSN 0378-5173--Print Journal Code: 7804127
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS
We investigated the application of Carbopol(R) (CP) as a novel coating material prepared with various grades of CP having different degrees of cross-linking and molecular weights. Viscosity and spray mist size of CP aqueous solutions at various concentrations of CP were measured. Core **tablets** containing theophylline (TP), as a model drug, were coated with CP at various coating ratios. The TP release profile from the CP-coated **tablets** was studied by the JP13 paddle method. CP **tablets** were prepared by compressing CP powder, and the swelling behavior of the CP **tablets** in JP 1st fluid, purified water, and JP 2nd fluid was observed. The spray mist size of all CP aqueous solutions was small at a concentration of 1% and below, and drastically increased over a concentration of 1%. This result suggests that the appropriate concentration of the CP solution for coating is 1% or below. Sustained release of TP from the CP-coated **tablets** at a coating ratio of only 3% was observed in the JP 1st fluid and purified water, although **fast release** was observed in the JP 2nd fluid. The **fast release** in the latter fluid may be due to the fact that CP is an acid material. These results suggest that it is feasible to control the **drug release** by use of an extremely small amount of CP coating and that CP is useful as a novel coating material.
Descriptors: *Polyvinyls--chemistry--CH; Bronchodilator Agents--chemistry --CH; Cross-Linking Reagents; Drug Carriers; **Particle Size** ; Solubility; **Tablets** , Enteric-Coated; Theophylline--chemistry--CH; Viscosity
CAS Registry No.: 0 (Bronchodilator Agents); 0 (Cross-Linking Reagents); 0 (Drug Carriers); 0 (Polyvinyls); 0 (Tablets, Enteric-Coated); 58-55-9 (Theophylline); 9007-20-9 (carboxypolymethylene)
Record Date Created: 20000725
Record Date Completed: 20000725

10/9/3 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12253064 PMID: 10937289
Technology to obtain sustained release characteristics of drugs after delivered to the colon.

Hu Z; Kimura G; Ito Y; Mawatari S; Shimokawa T; Yoshikawa H; Yoshikawa Y; Takada K

Department of Pharmacokinetics, Kyoto Pharmaceutical University, Japan.

Journal of drug targeting (SWITZERLAND) **1999** , 6 (6) p439-48, ISSN 1061-186X--Print Journal Code: 9312476

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

To determine the necessary technology by which sustained **drug release** is obtained after drug is delivered to the colon, two kinds of microcapsules were prepared and were filled in a pressure-controlled colon delivery capsule (PCDC). As a model drug 5-aminosalicylic acid (5-ASA) was used, because the target site of 5-ASA is the entire large intestine. 5-ASA was microencapsulated using a water-insoluble polymer, ethylcellulose (EC) or with pH-sensitive polymers, Eudragit L-100 or S-100 and encased in PCDC. The **particle size** of these microcapsules was around 800 microns and the loading efficiencies of 5-ASA were approximately 90%. In vitro dissolution tests were performed with the prepared microcapsules. The release rate of 5-ASA from the microcapsules was significantly prolonged as compared to 5-ASA powder, although there were no significant differences in the release rates between these microcapsules. By incorporating the 5-ASA microcapsules into PCDC, sustained release PCDCs for colon delivery were prepared and in vivo evaluation was performed using beagle dogs. As a **fast release** colon delivery system, PCDCs were prepared with 5-ASA powder suspended in suppository base. After **oral** administration of the test preparations to beagle dogs, plasma 5-ASA concentrations were measured and sustained release characteristics of 5-ASA from the test preparations were evaluated from the plasma 5-ASA concentration-time profiles. The first appearance time of 5-ASA into the systemic circulation after **oral** administration were 3 h for all the colon delivery preparations and it was thought that these test preparations were delivered to the colon. Both EC microcapsules and Eudragit S-100/RS-100 microcapsules in PCDC showed longer the mean residence time MRT, 8.2 +/- 0.6 h and 8.7 +/- 0.9 h, than Eudragit L-100/RS-100 microcapsules in PCDC where the MRT was 6.6 +/- 0.2 h. Since PCDCs containing 5-ASA powder exhibited a MRT of 7.0 +/- 1.0 h, these two types of preparations have suggested sustained release characteristics.

Tags: Male

Descriptors: *Colon--metabolism--ME; *Delayed-Action Preparations; Algorithms; Animals; Area Under Curve; Capsules; Cellulose--analogs and derivatives--AA; Chemistry, Physical; Dogs; Drug Delivery Systems; Excipients; Hydrogen-Ion Concentration; Injections, Intravenous; Mesalamine --blood--BL; Mesalamine--pharmacokinetics--PK; Polymethacrylic Acids; Powders; Solubility

CAS Registry No.: 0 (Capsules); 0 (Delayed-Action Preparations); 0 (Excipients); 0 (Polymethacrylic Acids); 0 (Powders); 25086-15-1 (methylmethacrylate-methacrylic acid copolymer); 89-57-6 (Mesalamine); 9004-34-6 (Cellulose); 9004-57-3 (ethyl cellulose)

Record Date Created: 20000829

Record Date Completed: 20000829

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Set	Items	Description
S1	39949	PARTICLE()SIZE
S2	9496	DRUG()RELEASE
S3	1119	S1 AND S2
S4	2714	IMMEDIATE()RELEASE OR FAST()RELEASE
S5	1119	S1 AND S2 AND S3
S6	741667	ORAL OR PERORAL

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S7      779168   ORAL OR PERORAL OR TABLET?
S8           8   S1 AND S2 AND S4 AND S7
S9           6   RD  (unique items)
S10          3   S9 AND PY<=2001
?
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ds

Set	Items	Description
S1	39949	PARTICLE()SIZE
S2	57832	CRYSTALLINE
S3	266879	CRYSTAL?
S4	5134751	DRUG OR PHARMACEUTICAL
S5	741667	ORAL OR PERORAL
S6	2714	IMMEDIATE()RELEASE OR FAST()RELEASE
S7	35	S6 AND S3
S8	27	S6 AND S3 AND S4
S9	20	RD (unique items)
S10	3	S6 AND S3 AND S4 AND S1
S11	2	RD (unique items)

? t s11/full/all

11/9/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0015240638 BIOSIS NO.: 200500147703
Observations in simultaneous microencapsulation of 5-fluorouracil and leucovorin for combined pH-dependent release
AUTHOR: Lamprecht Alf; Yamamoto Hiromitsu; Takeuchi Hirofumi; Kawashima Yoshiaki (Reprint)
AUTHOR ADDRESS: Lab Pharmaceut Engn, Gifu Pharmaceut Univ, 5-6-1 Mitahora Higashi, Gifu, 5028585, Japan**Japan
AUTHOR E-MAIL ADDRESS: yoshiaki@gifu-pu.ac.jp
JOURNAL: European Journal of Pharmaceutics and Biopharmaceutics 59 (2): p 367-371 February 2005 2005
MEDIUM: print
ISSN: 0939-6411 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: 5-Fluorouracil (5-FU) in combination with leucovorin (LV) is nowadays the standard treatment in colon cancer and would be a candidate to be delivered orally to the colon. Eudragit P-4135F or Eudragit RS100 were used separately to prepare microspheres by an oil/oil emulsification process trapping 5-FU and LV simultaneously. Scanning electron microscopy permitted a structural analysis, process parameters were analyzed and **drug** loading and release profiles were recorded. **Particle size** varied between 123 (RS100) and 146 Pm (P-4135F). Generally, higher encapsulation rates were found with RS100 (5-FU, 60.3 +/- 9.7%; LV, 81.4 +/- 8.6%) compared to P-4135F (5-FU, 48.3 +/- 2.0%; LV, 55.4 +/- 2.7%). Microparticles made from Eudragit RS100 released the incorporated **drug** combination within 8 h not exhibiting general differences between the kinetics of both drugs. P-4135F was found to maintain the undesired 5-FU release at pH 6.8 lower than 25% within 4 h. while at pH 7.4, a nearly **immediate release** (within 15 min) was observed. Although the release was similar at pH 7.4, at pH 6.8 LV showed a distinct initial **drug** loss of about 60% and a complete release within 2 h. SEM analyses revealed a substantial presence of LV **crystals** on the particle surface provoking a distinct burst effect of LV. These observations were concluded to be related to the high lipophilicity of P-4135F provoking a separation between P-4135F and LV during the preparation process. Copyright 2004 Elsevier B.V. All rights reserved.

REGISTRY NUMBERS: 51-21-8: 5-fluorouracil; 33434-24-1: Eudragit RS100; 58-05-9: leucovorin

DESCRIPTORS:
MAJOR CONCEPTS: Equipment Apparatus Devices and Instrumentation; Gastroenterology--Human Medicine, Medical Sciences; Methods and Techniques; Oncology--Human Medicine, Medical Sciences; Pharmacology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)
ORGANISMS: PARTS ETC: colon--digestive system
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: colon cancer--digestive system disease, neoplastic disease, **drug** therapy, prevention and control
MESH TERMS: Colonic Neoplasms (MeSH)
CHEMICALS & BIOCHEMICALS: 5-fluorouracil {5-FU}--antineoplastic- **drug** , **drug** regimen, oral administration, pharmacokinetics; Eudragit P-4135F; Eudragit RS100; leucovorin {LV}--antineoplastic- **drug** , **drug** regimen, oral administration, pharmacokinetics
METHODS & EQUIPMENT: Eudragit P-4135F microsphere-- **drug** delivery device ; Eudragit RS100 microsphere-- **drug** delivery device; scanning electron microscopy {SEM} {scanning electron microscopy}--imaging and microscopy techniques, laboratory techniques
MISCELLANEOUS TERMS: burst effect; combined pH-dependent **drug** release ; **drug** loading profile; **drug** release profile; encapsulation rate; lipophilicity; **particle size**
CONCEPT CODES:
10060 Biochemistry studies - General
10062 Biochemistry studies - Nucleic acids, purines and pyrimidines
12512 Pathology - Therapy
14004 Digestive system - Physiology and biochemistry
14006 Digestive system - Pathology
22002 Pharmacology - General
22003 Pharmacology - Drug metabolism and metabolic stimulators
22005 Pharmacology - Clinical pharmacology
24004 Neoplasms - Pathology, clinical aspects and systemic effects
24008 Neoplasms - Therapeutic agents and therapy
BIOSYSTEMATIC CODES:
86215 Hominidae

11/9/2 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14234286 PMID: 12661666
Etanidazole-loaded microspheres fabricated by spray-drying different poly(lactide/glycolide) polymers: effects on microsphere properties.
Wang Fang-Jing; Wang Chi-Hwa
Department of Chemical and Environmental Engineering, National University of Singapore, 4 Engineering Drive 4, Singapore 117576, Republic of Singapore.
Journal of biomaterials science. Polymer edition (Netherlands) 2003, 14 (2) p157-83, ISSN 0920-5063--Print Journal Code: 9007393
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In this work, a spraying technique was used to encapsulate etanidazole (a hypoxic radiosensitizer) into different poly(lactide/glycolide) polymers.

The properties of the obtained microspheres, especially the **particle size** and distribution, morphology and release rate were investigated. Unexpectedly, poly(L-lactide) (PLLA) shows a **fast release** rate, comparable to PLGA 50: 50, due to the dissociation of the microspheres although the release rate of the spray-dried microspheres of other polymers decreases with increasing lactide ratio. It is also interesting to note that, contrary to the viscosity sequence of the polymer solutions, the **particle size** of the microspheres decreases in the order PLGA 50: 50, PLGA 65: 35, PLGA 85: 15 and PDLA. The morphology of microspheres can be affected by polymer properties (e.g. lactide/glycolide ratio, molecular weight, **crystallinity** and Tg) and fabrication conditions (e.g. solvent and polymer concentration to be sprayed). Although most of the microspheres fabricated by EA have a donghnut-like shape with smooth surface, it is possible to obtain spherical particles by choosing proper polymer type and polymer concentration. A further examination of the mechanisms of the atomization process and the solvent evaporation process reveals their respective effect on droplet formation and particle formation, both of which are essential for the spray-drying technique. It is found that polymer phase transition (affected by the polymer solubility) and its subsequent solvent evaporation processes can finally determine the morphology and the **particle size** of the spray-dried particles made from different polymers. In essence, the lactide/glycolide ratio of the polymers plays a more important role in affecting the properties of the spray-dried microspheres.

Descriptors: *Biocompatible Materials; *Etanidazole; *Microspheres; *Polyglactin 910; Calorimetry, Differential Scanning; Delayed-Action Preparations; **Drug** Carriers; Microscopy, Electron, Scanning; Polyglactin 910--chemistry--CH; Radiation-Sensitizing Agents; Research Support, Non-U.S. Gov't; Viscosity

CAS Registry No.: 0 (Biocompatible Materials); 0 (Delayed-Action Preparations); 0 (Drug Carriers); 0 (Radiation-Sensitizing Agents); 22668-01-5 (Etanidazole); 34346-01-5 (Polyglactin 910)

Record Date Created: 20030328

Record Date Completed: 20031120

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Set	Items	Description
S1	39949	PARTICLE()SIZE
S2	57832	CRYSTALLINE
S3	266879	CRYSTAL?
S4	5134751	DRUG OR PHARMACEUTICAL
S5	741667	ORAL OR PERORAL
S6	2714	IMMEDIATE()RELEASE OR FAST()RELEASE
S7	35	S6 AND S3
S8	27	S6 AND S3 AND S4
S9	20	RD (unique items)
S10	3	S6 AND S3 AND S4 AND S1
S11	2	RD (unique items)